

2. Page 16, line 20 to 30 and page 17 lines 1 to 15, change to read:

NYX encodes a 481 amino acid protein, herein called nyctalopin, which has sequence similarity with members of the superfamily of proteins containing tandem arrays of the leucine-rich repeat (LRR) motif [10,13]. Such proteins are known to function in protein-protein interactions, especially in matrix assembly, and therefore nyctalopin may possibly be mediating specific neural connections between cells in the retina. Moreover, the presence of the 24 amino acid consensus: x-x-I/V/L-x-x-x-x-F/P/L-x-x-L/P-x-x-L-x-x-L/I-x-L-x-x-N-x-I/L (where I,V,L,F,P and N are single letter amino acid codes and "x" represents any amino acid) in the core protein with cysteine clusters flanking the LRR domain (see Figure 3B) **[SEQ ID NO: 2]**, qualifies nyctalopin as a new member of the subfamily of small leucine-rich proteoglycans (SLRPs) [10]. From a homology comparison of nyctalopin with other SLRP proteins, it is evident that nyctalopin is a unique member of this subfamily and the LRR superfamily in general. Nyctalopin has five putative consensus sequences (N-X-(S/T)) necessary for substitution by N-linked oligosaccharides or keratan sulfate [14], three of these sequences lie within the LRR region. The NH₂-terminal end of nyctalopin is predicted [15] to contain a membrane signal peptide with a putative cleavage site between amino acid 23 and 24, AWA-VG (Figure 3). In addition, the carboxyl-terminal region of nyctalopin contains a GPI-anchor signal sequence, including the requisite GPI N-terminal signal sequence (amino acids 339 to 379), the C-terminal hydrophobic region (last 22 amino acids) and a potential cleavage site at amino acids 445-447 [16] (Fig. 3B) **[SEQ ID NO: 2]**. The identification of these sites was accomplished at the website www.expasy.ch/tools, and is well known to those skilled in the art. Thus, *NYX* codes for a GPI-anchored proteoglycan with a putative membrane signal peptide. Without being limited to a theory, these results suggest that the clinical features of complete X-linked CSNB can be explained by the presence of a mutant nyctalopin (or entire absence of nyctalopin) causing the disruption of selected connections or interactions between retinal neurons, including those of the retinal ON-bipolar pathway, possibly during early stages of embryonic development.

3. Page 22 lines 28 to 30 and page 23 lines 1 to 10, change to read:

Fourteen different mutations have been identified in *NYX*, none of which are observed in chromosomes from normal individuals. In nyctalopin, there are 11 leucine-rich repeats, which

are all highly conserved with respect to the consensus sequence in SLRPs, and these are flanked by cysteine clusters (see Figure 3B) [SEQ ID NO: 2] [10]. The deletion of a portion of the cysteine cluster in the amino-terminal portion of nyctalopin appears to be responsible for complete X-linked CSNB in six families, which highlights the importance of this conserved region. The mutation that causes a stop codon on the carboxyl-terminal side of the leucine-rich repeats and another cysteine cluster, likely affects the ability of the protein to anchor in the membrane, as the protein portion on the carboxyl-terminal side of this mutation is presumed to be important for GPI anchoring nyctalopin in the cellular membrane. Mutations that replace a consensus amino acid with another amino acid are presumed to disrupt an essential amino acid function. Mutations that result in the insertion (or deletion) of amino acids in the protein are presumed to alter the folding of the protein

4. Page 30, lines 6 to 12, change to read:

Six other families were found to have an in-phase 24-nt deletion that results in the loss of eight amino acids - RACPAACA (see Figure 5B). Six of these amino acids form part of a conserved cysteine-cluster on the amino-terminal side of the leucine-rich repeats, as shown in Figure 3B [SEQ ID NO: 2]. Haplotype analysis of X chromosomes with this deletion mutation from each of the six families revealed nearly identical haplotypes, suggesting that these families share a common founder mutation. In three families, insertion mutations representing duplications of adjacent protein sequence add either six or three amino acids (Figure 3B) [SEQ ID NO: 2].

AMENDMENTS TO THE CLAIMS

1. Please amend claims to read as follows

Claims 1-24 (Cancelled)

Claim 25 (Previously Added) An isolated or recombinant DNA molecule encoding the amino acid sequence of SEQ ID NO: 2.

Claim 26 (Previously Added) The DNA molecule of claim 25 comprising a nucleotide sequence corresponding to SEQ ID NO: 1.